

Appl. No. : 09/981,783
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AMENDMENTS TO THE SPECIFICATION

Please replace paragraph number [0005] with the following rewritten paragraph:

[0005] Fig. 3 is an enlarged side view of a portion of a filter device of the type illustrated in Fig. 1 showing ~~four~~seven elongated hollow fibers secured along the hollow tubes;

Please replace paragraph number [00011] with the following rewritten paragraph:

[0011] The elongated hollow microporous fibers used in the filter device are the asymmetrical wall fibers disclosed in U.S. Patent No. 6,802,820 ~~Application Serial No. 09/549,131~~ ~~filed April 13, 2000~~, the descriptions of which are incorporated herein by reference. The morphology of the fiber walls is asymmetrical between the inner fiber lumen and the outer fiber wall which is in direct contact with the blood flowing in the vasculature in which the device is implanted. The filtration performance of such a device is a function of the filter surface of the exposed fibers whereby consideration is given to use larger diameter fibers and to maximize the number of fibers. Thus, it is desirable to use as many individual fibers along the hollow core tubes of the filter device as is practical while maintaining separation of the individual fibers to provide for fluid flow therebetween, and to maximize the amount of outer fiber surface exposed to blood flowing along the length of the filter device. Moreover, the fibers are secured along the length of the hollow tubes in such a manner as to form a fluid flow space between the fibers and the tubes. Again, however, the length of the filter device as well as the overall cross-sectional dimension are tailored or dictated by the blood vessel in which the device is to be used so as to avoid substantial interference with blood flow through the vessel while at the same time be efficient to achieve the intended flow rate of separated plasma.

Please replace paragraph number [0015] with the following rewritten paragraph:

[0015] The fiber wall structure of the elongated microporous fibers is asymmetrical between the inner wall surface extending along the interior fiber lumen and the outer fiber wall surface exposed to blood in the vessel in which the filter device is implanted. The fiber wall at or adjacent to the outer wall surface has a higher mass density than the mass density adjacent to or at the inner wall surface. The mass density is a function of the average nominal pore size. Such asymmetric fiber wall morphology is illustrated in Figs. 7 and 8, Fig 7 showing a scanning

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electron microscopy (SEM) image of a cross-section of the fiber at 100 μm magnification. Fig. 8 shows a portion of the Fig. 7 fiber wall cross-section at a magnification of 400 μm . It will be observed that the structure of the fiber from the outer surface to the lumen is a continuous change in mass density whereby the pore size gradually changes between these fiber wall surfaces. However, it is convenient to describe the different mass density as sections or zones of the wall area having an average nominal pore size or average pore diameter, each zone having a different average nominal pore size. The walls may be characterized by two or more zones, for example 2, 3, or 4 or more mass density zones. The hollow fibers shown in Figs. 7 and 8 are also shown and described in the aforesaid application Serial No. 09/549,131 (TRANSVI.007A) U.S. Patent No. 6,802,820. In the fibers, the outer surface of the membrane, zone 1, has the highest mass density characterized by smaller average pore diameters. The outer zone forms the fiber interface with the permeate blood flow by determining filtration characteristics including the composition and components of separated plasma and controlling fiber membrane performance. Thus, zone 1 is the principle filtration portion of the fiber wall for controlling the trans-membrane flux (TMF) for excluding even the smallest cells in the blood, the platelets, having a diameter of about 1 μm . Nominal average pore diameters in zone 1 are between about 0.3 μm and about 1 μm , and preferably range from about 0.4 μm to about 0.8 μm . A preferred filtration sizing has a cutoff of about 0.6 μm to about 0.8 μm . Zones 2 and 3 are designed to decrease the flow path tortuosity and maintain the structural integrity required of the fiber exposed to physical conditions within the body. Pore size distribution in these zones ranges gradually from about 0.8 μm to about 1.2 μm and from about 1.2 μm to about 2.0 μm . Zone 2, having some flux-controlling pores, is principally to provide structural strength to the fiber as well as acting as a conduit for exudate flow to zone 3, also providing structure and enlarged pores for reducing the hydraulic resistance and providing a fluid conduit to the fiber lumen. The interior zones have little filtration function. Zone 4, representing the largest area having relatively large voids and pore diameters with little solid structure, has the primary function of a major reduction of hydraulic resistance through the membrane and defines the fiber inner lumen surface. Nominal average pore diameters in this lowest mass density zone are between about 1 μm and about 60 μm , and preferably between about 2 μm and about 6 μm . A typical fiber as shown has an OD of about 650 μm , an ID of about 250 μm and a wall thickness of about 250 μm . However, such dimensions are by way of

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example only. The fiber wall morphology, voids and pores may be further observed in Applicant's aforesaid ~~co-pending application Serial No. 09/549,131~~ U.S. Patent No. 6,802,820, with figures illustrating the structures at magnifications of 1,000 μm and 5,000 μm .

Please replace paragraph number [0017] with the following rewritten paragraph:

[0017] The filter device is used for carrying out *in-vivo* plasmapheresis in combination with a multiple lumen catheter, preferably a triple lumen catheter as illustrated in Fig. 6. The catheter is of a suitable length to provide for implanting or installing the filter device into the appropriate vessel of the patient, e.g., the inferior vena cava, between the diaphragm and the iliac junction via the femoral vein, jugular vein or subclavian vein. The catheter 20 may be secured to the proximal end 17 of the filter device 10 by a suitable method, e.g., using a suitable adhesive and an injection-molded connector 19. The catheter 20 has an access lumen 26 which is in open fluid communication with the interior of elongated hollow tubes 14 and 16 of the filter device. Return lumen 22 is occluded or blocked off at the distal end of the catheter 20, and is provided with one or more ports through the catheter wall near the distal end of the catheter whereby treated plasma may be returned to the patient. Backflush lumen 24 is also in open fluid communication with the interior of the hollow tubes 14 and 16 through which periodic backflush fluid is directed for preventing occlusion of the hollow fiber membrane caused by blood components. Such backflush procedure and apparatus are discussed in detail in ~~co-pending application Serial No. 09/754,773, filed January 4, 2001 (TRANSVI.008A)~~ U.S. Patent No. 6,659,973, the description of which is incorporated herein by reference. The proximal end of the triple lumen catheter is secured to tubing components of a plasma separation system, such as disclosed in the aforesaid ~~co-pending application (09/754,773)~~ U.S. Patent No. 6,659,973. The system includes plasma treatment apparatus for removing and/or separating selected plasma components and a fluid control assembly for directing plasma from the catheter to the treatment apparatus and return to the patient. The fluid control assembly also includes a pump for pumping plasma from the catheter to the treatment apparatus, a source of backflush fluid and a pump for pumping backflush fluid to the backflush lumen of the catheter. The fluid control apparatus also includes a microprocessor/controller for operating the pumps and controlling plasma flow rates and backflush fluid pressures, and backflush pumping intervals. The plasma treatment apparatus may be a single or multiple stage dialysate filter assembly or cascade membrane filters, absorbent

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cartridges, specialized adsorbent columns, chemical process or extraction assembly, or combinations, known to those skilled in the art.